UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/809,662	03/15/2001	Steven Stice	235.0032 0101	5744

7590 11/06/2002

Mueting Raasch & Gebhardt P.A.
P.O. Box 581415
Minneapolis, MN 55458

EXAMINER	
CROUCH, DEBORAH	

ART UNIT	PAPER NUMBER
1632	10

DATE MAILED: 11/06/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	**Application No.**	**Applicant(s)**	
	09/809,662	STICE, STEVEN	
	Examiner	**Art Unit**	
	Deborah Crouch, Ph.D.	1632	

-- The MAILING DATE of this communicati n appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 July 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *197-230* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *197-230* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4* .
4) ☒ Interview Summary (PTO-413) Paper No(s). *10 & 11* .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

The preliminary amendment filed October 2, 2002 in paper no. 8 has been entered. Claims 197-230 are pending.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 197-230 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of producing a cloned non-human mammalian NT embryo, the method comprising introducing a donor nucleus into an oocyte enucleated either before or after transfer of the donor nucleus to yield a cloned nonhuman mammalian NT embryo and activating the embryo, wherein the donor nucleus introduced into the oocyte is obtained from a donor cell that is arrested at late G1 phase and methods of producing a cloned nonhuman mammal comprising transferring the embryo to a host female of the same species, does not reasonably provide enablement for a method of producing a cloned non-human mammalian NT embryo, the method comprising introducing a donor genetic material into an oocyte to yield a cloned nonhuman mammalian NT embryo, wherein the donor genetic material introduced into the oocyte is obtained from a donor cell that is arrested at late G1 phase. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claims as presently written do not specify that the donor nucleus, the oocyte and the surrogate mother all need to be from the same species. The art at the time of filing taught that in the production of chimeric goat-sheep, there were biases towards chimeras whose genotype and phenotype was most like that of the recipient, and that the successful

production of chimeras resided in the neutralization of incompatibility between the chimeric embryos (Fehilly et al (1985), page 221, parag. 1). Further the production of transpecies embryos was regarded as unpredictable at the time of filing. Attempt so an oocyte from a bovine (Bos) as the recipient cell for nuclear transfer protocols, where the donor cell nucleus is from an unrelated species, embryo development underwent an early arrest (Meirelles et al (2001), page 351, col. 2, parag. 2, lines 1-4). The early arrest was attributed to incompatibility between the nuclear and mitochondrial genes (Meirelles et al, page 352, col. 1, lines 4-7). From these results, decreased proliferation and development capacity is observed the greater the phylogenetic distance between donor and host cell. Thus the specification does not enable the claim as there is no enabled use for any chimeric, and the specification does not provide sufficient guidance to the production of a particular chimeric non-human animal. To be clear on the record, when the examiner states "species" what is meant by separate species is that bovine, ovine, porcine, caprine, equine and the like are individual species, or the taxonomical genus names, *Bos*, *Sus* and the like are separate species. Further, this type of definition is supported at least by the findings of Meirelles et al. (see abstract, and page 354, figure 3)

The only type of donor genetic material enabled is a donor nucleus. The specification only defines donor genetic material as being a cell or cell nucleus. The use of isolated chromosomes would be unpredictable as the methods of isolating donor chromosomes frequently damages the chromosomes. Intact chromosomes are needed for nuclear transfer.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 197 and 220-225 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 221 and 223-225 do not further limit claim 197. Claim 197 is drawn to a method of producing a cloned nonhuman NT embryo. The production of a cloned mammal is not a further limitation of a method of producing an NT embryo. Applicant needs to rewrite claims 221 and 223-225 as methods of producing a cloned nonhuman mammal, using the embryo made by the method of claim 197.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 197, 199, 200, 206, 208, 209, 212, 214, 220, 222 and 227 are rejected under 35 U.S.C. 102(b) as being clearly by Collas et al (1992) Biol. Reprod. 46, 492-500.

Collas teaches the production of rabbit NT embryos where the donor cell was synchronized at the G1/S boundary (page 494, col. 1-2, bridg. Parag.). Collas teaches the

dissaggregation of rabbit embryos into their blastomere components and incubating the blastomeres, first in colcemid followed by release and synchronization at the G1/S boundary by incubation in aphidicolin (page 494, col. 1, parag. 3, line 7 to col. 2, line 2; and col. 2, parag. 1, lines 1-8). Collas refers to this procedure as "arrest" of embryos in G1 (page 494, col. 2, parag. 2, lines 6-10). Oocyte were enucleated prior to transfer of the donor nucleus and the oocyte-blastomere complex was fused and activation was concomitant with fusion, after the nucleus was inserted into the oocyte (page 493, col. 1, parag. 4 to col. 2, lines 9). The fusion was after insertion, but about the same time. NT embryos prepared with G1 nuclei, proceeded in vitro to 2-cell, 4-cell, morula and blastocyst stages (page 498, Table 5). Thus, Collas clearly anticipates the claimed invention.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 197, 199, 201, 202, 204, 218 and 219 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent 5,945,577 issued August 31, 1999 (Stice) in view of Collas et al (1992) Biol. Reprod. 46, 492-500.

Stice teaches methods of cloning by nuclear transfer where the donor cell can be fibroblast, an epithelial cells, a hematopoietic cells or a lymphocyte, which also represent adult or cultured cells, or that the donor cell can be from ectoderm, mesoderm or endoderm, which are late stage embryo cells (col. 8, lines 4-15). Stice specifically describes the culture of fetal fibroblast cells, which are then used as nuclear donors (col. 15, liens 51 to col. 16, line 11 and col. 16, lines 57-60). Stice states that the method cloning via nuclear

transfer can be used to clone pigs and bovines (claim 13). Stice teaches that the insertion of a isolated nucleus in some instances is preferable (col. 10, lines 10-15). Collas teaches the production of rabbit NT embryos by transferring a donor blastomere cell that had been synchronized at the G1/S boundary into an enucleated oocyte (page 494, col. 1-2, bridg. Parag.). Collas teaches the dissaggregation of rabbit embryos into their blastomere components and incubating the blastomeres, first in colcemid followed by release and synchronization at the G1/S boundary by incubation in aphidicolin (page 494, col. 1, parag. 3, line 7 to col. 2, line 2; and col. 2, parag. 1, lines 1-8). Collas refers to this procedure as "arrest" of embryos in G1 (page 494, col. 2, parag. 2, lines 6-10). Collas offers motivation in stating that an enhanced rate of development was seen in nuclear transfer embryos to blastocysts with donor nuclei in the G1 phase, 71% (abstract). Thus, it would have been obvious to the ordinary artisan to modify the method of producing NT embryos as taught by Stice where the donor cell was from a proliferating cell culture with the method of producing cloned NT embryos where the donor cells were arrested in G1 prior to transfer as taught by Collas to obtain a greater number to blastocysts. Stice offers motivation by teaching that blastocyst production by the method disclosed therein was 10% (col. 17, lines 40-41).

Claims 197, 202 and 203 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent 5,945,577 issued August 31, 1999 (Stice) in view of Collas et al (1992) Biol. Reprod. 46, 492-500 and Wakayama et al (1998) Nature 394, pages 369-374.

Stice teaches methods of cloning by nuclear transfer where the donor cell can be fibroblast, an epithelial cells, a hematopoietic cells or a lymphocyte, which also represent adult or cultured cells, or that the donor cell can be from ectoderm, mesoderm or endoderm, which are late stage embryo cells (col. 8, lines 4-15). Stice specifically describes the culture of fetal fibroblast cells, which are then used as nuclear donors (col. 15, liens 51

to col. 16, line 11 and col. 16, lines 57-60). Stice states that the method cloning via nuclear transfer can be used to clone pigs and bovines (claim 13). Stice teaches that the insertion of a isolated nucleus in some instances is preferable (col. 10, lines 10-15). Collas teaches the production of rabbit NT embryos by transferring a donor blastomere cell that had been synchronized at the G1/S boundary into an enucleated oocyte (page 494, col. 1-2, bridg. Parag.). Collas teaches the dissaggregation of rabbit embryos into their blastomere components and incubating the blastomeres, first in colcemid followed by release and synchronization at the G1/S boundary by incubation in aphidicolin (page 494, col. 1, parag. 3, line 7 to col. 2, line 2; and col. 2, parag. 1, lines 1-8). Collas refers to this procedure as "arrest" of embryos in G1 (page 494, col. 2, parag. 2, lines 6-10). Collas offers motivation in stating that an enhanced rate of development was seen in nuclear transfer embryos to blastocysts with donor nuclei in the G1 phase, 71% (abstract). Wakayama teaches the production of cloned mice using cumulus cells as nuclear donors (page 370, Table 1). Stice offers motivation by teaching that blastocyst production by the method disclosed therein was 10% (col. 17, lines 40-41). Collas offers motivation in stating that an enhanced rate of development was seen in nuclear transfer embryos to blastocysts with donor nuclei in the G1 phase, 71% (abstract). Wakayama offers motivation in that a blastocyst development rate of 39% was reported (page 370, Table 1). Thus, it would have been obvious to the ordinary artisan to modify the method of producing NT embryos as taught by Stice where the donor cell was from a proliferating cell culture with the method of producing cloned NT embryos where the donor cells were arrested in G1 prior to transfer as taught by Collas, where the donor cells were cumulus cells, a taught by Wakayama in order to obtain a greater number to blastocysts.

Claims 197 and 205 are rejected under 35 U.S.C. 103(a) as being unpatentable over Collas et al (1992) Biol. Reprod. 46, pages 492-500 in view of Cibelli et al (1998) Science 280, pages 1256-1259.

Collas teaches the production of rabbit NT embryos where the donor cell was synchronized at the G1/S boundary (page 494, col. 1-2, bridg. Parag.). Collas teaches the dissaggregation of rabbit embryos into their blastomere components and incubating the blastomeres, first in colcemid followed by release and synchronization at the G1/S boundary by incubation in aphidicolin (page 494, col. 1, parag. 3, line 7 to col. 2, line 2; and col. 2, parag. 1, lines 1-8). Collas refers to this procedure as "arrest" of embryos in G1 (page 494, col. 2, parag. 2, lines 6-10). Collas does not teach the production of NT embryos where the donor nucleus contains transgenic DNA. However, Cibelli teaches the production of NT embryos where the donor nucleus contains a β-galactosidase-neomycin resistance fusion gene driven by a CMV promoter (page 1256, col. 3, parag. 1, lines 1-16 and page 1257, col. 1, parag. 1, lines 1-3). Cibelli offers motivation in stating that the donor cells were not synchronized in G1, but that FACS analysis showed that 56% of the cells were in G1 and that this would provide a large population that could support development (page 1257, col. 3, parag. 1). Cibelli also states that the donor cells should be in G1 (page 1256, col. 3, lines 7-10). Collas offers motivation in stating that a high rate of development to the blastocyst stage was obtained using G1 synchronized donors (page 499, col. 1parag. 3, lines 4-7).

Claims 197, 206, 212 and 213 rejected under 35 U.S.C. 103(a) as being unpatentable over Collas et al (1992) Biol. Reprod. 46, 492-500 in view of Yang et al, (1992) Biol. Reprod. 46, suppl. No. 1, page 117, Abs. 268.

Collas teaches the production of rabbit NT embryos where the donor cell was synchronized at the G1/S boundary (page 494, col. 1-2, bridg. Parag.). Collas teaches the

disaggregation of rabbit embryos into their blastomere components and incubating the blastomeres, first in colcemid followed by release and synchronization at the G1/S boundary by incubation in aphidicolin (page 494, col. 1, parag. 3, line 7 to col. 2, line 2; and col. 2, parag. 1, lines 1-8). Collas refers to this procedure as "arrest" of embryos in G1 (page 494, col. 2, parag. 2, lines 6-10). Yang teaches methods of activating matured oocytes in the presence of cyclohexamide (lines 4-6). Yang teaches that cyclohexamide and electrofusion combined resulted in the activation of 90% of the oocytes (lines 20-27). Collas offers motivation in stating that an enhanced rate of development was seen in nuclear transfer embryos to blastocysts with donor nuclei in the G1 phase, 71% (abstract). Thus, it would have been obvious to the ordinary artisan to modify the method of producing NT embryos as taught by Collas with the method of activation described by Yang to prevent the meiotic arrest of mater oocytes so that a greater number of functional NT units could be produced.

Claims 197, 206 and 207 are rejected under 35 U.S.C. 103(a) as being unpatentable over Collas et al (1992) Biol. Reprod. 46, 492-500 in view of Campbell et al (1996) Nature 380, 64-66.

Collas teaches the production of rabbit NT embryos where the donor cell was synchronized at the G1/S boundary (page 494, col. 1-2, bridg. Parag.). Collas teaches the dissaggregation of rabbit embryos into their blastomere components and incubating the blastomeres, first in colcemid followed by release and synchronization at the G1/S boundary by incubation in aphidicolin (page 494, col. 1, parag. 3, line 7 to col. 2, line 2; and col. 2, parag. 1, lines 1-8). Collas refers to this procedure as "arrest" of embryos in G1 (page 494, col. 2, parag. 2, lines 6-10). Campbell teaches the "preactivation" of oocytes, prior to introduction of a donor nucleus (page 64, col.2 , parag. 1, lines 13-16). Campbell offers motivation in stating that the prior activation of a recipient oocyte overcomes donor cell

cycle stage effects by reducing MPF activity and subsequent donor chromosome damage (page 64, col. 1, parag. 3, lines 1-9). Thus at the time of the instant invention, it would have been obvious to the ordinary artisan to modify the method of Collas by preactivating the recipient oocyte so that MPF activity would be lower and lessen the chance of damage to the donor chromosomes as taught by Campbell.

Claims 197, 206 and 210 rejected under 35 U.S.C. 103(a) as being unpatentable over Collas et al (1992) Biol. Reprod. 46, 492-500 in view of Campbell et al (1996) Nature 380, 64-66.

Collas teaches the production of rabbit NT embryos where the donor cell was synchronized at the G1/S boundary (page 494, col. 1-2, bridg. Parag.). Collas teaches the dissaggregation of rabbit embryos into their blastomere components and incubating the blastomeres, first in colcemid followed by release and synchronization at the G1/S boundary by incubation in aphidicolin (page 494, col. 1, parag. 3, line 7 to col. 2, line 2; and col. 2, parag. 1, lines 1-8). Collas refers to this procedure as "arrest" of embryos in G1 (page 494, col. 2, parag. 2, lines 6-10). Campbell teaches the "preactivation" of oocytes, prior to introduction of a donor nucleus (page 64, col.2 , parag. 1, lines 13-16). Campbell offers motivation in stating that the prior activation of a recipient oocyte overcomes donor cell cycle stage effects by reducing MPF activity and subsequent donor chromosome damage (page 64, col. 1, parag. 3, lines 1-9). Thus at the time of the instant invention, it would

Claims 197, 220 and 221 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent 6,235,969 issued May 22, 2001 (Stice) in view of Collas et al (1992) Biol. Reprod. 46, 492-500.

Stice teaches the use of synchronized G1 fibroblast as nuclear donors in the production of NT porcine embryos (col. 17, lines 48-49). Stice teaches the transfer of 20-30

NT units directly to a host pig (col. 19, lines 33-37). Collas teaches the production of rabbit NT embryos where the donor cell was synchronized at the G1/S boundary (page 494, col. 1-2, bridg. Parag.). Collas teaches the dissaggregation of rabbit embryos into their blastomere components and incubating the blastomeres, first in colcemid followed by release and synchronization at the G1/S boundary by incubation in aphidicolin (page 494, col. 1, parag. 3, line 7 to col. 2, line 2; and col. 2, parag. 1, lines 1-8). Collas refers to this procedure as "arrest" of embryos in G1 (page 494, col. 2, parag. 2, lines 6-10). Thus at the time of the instant invention, it would have been obvious to the ordinary artisan to modify the of producing pigs as taught by Stice by incubating donor fibroblasts in the presence of aphidicolin to synchronize fibroblast cells in G1.

Claims 197, 220 and 222-224 are rejected under 35 U.S.C. 103(a) as being unpatentable over Collas et al (1992) Biol. Reprod. 46, 492-500 in view of Yang et al (1992) Biol. Reprod. 47, 636-643.

Collas teaches the production of rabbit NT embryos by transferring a donor blastomere cell that had been synchronized at the G1/S boundary into an enucleated oocyte (page 494, col. 1-2, bridg. Parag.). Collas teaches the dissaggregation of rabbit embryos into their blastomere components and incubating the blastomeres, first in colcemid followed by release and synchronization at the G1/S boundary by incubation in aphidicolin (page 494, col. 1, parag. 3, line 7 to col. 2, line 2; and col. 2, parag. 1, lines 1-8). Collas refers to this procedure as "arrest" of embryos in G1 (page 494, col. 2, parag. 2, lines 6-10). Yang teaches the production of rabbit young by nuclear transfer (page 642, Table 4). Collas offers motivation in stating that an enhanced rate of development was seen in nuclear transfer embryos to blastocysts with donor nuclei in the G1 phase, 71% (abstract). Yang offers motivation in stating that rabbits are a relevant model in which to study nuclear transfer

(page 640, col. 2, parag. 3, lines 1-5). Thus, it would have been obvious to the ordinary artisan to modify the method of producing cloned NT embryos where the donor cells were arrested in G1 prior to transfer as taught by Collas, and Yang teaching the production of cloned rabbits by nuclear transfer in order to obtain a greater number of blastocysts for transfer to a surrogate rabbit.

Claims 197 and 226 are rejected under 35 U.S.C. 103(a) as being unpatentable over Collas et al (1992) Biol. Reprod. 46, 492-500 in view of Alessi et al (1998) Exp. Cell Res. 245, 8-18 in view of U.S. Patent 5,945,577 issued August 31, 1999 (Stice).

Collas teaches the production of rabbit NT embryos by transferring a donor blastomere cell that had been synchronized at the G1/S boundary into an enucleated oocyte (page 494, col. 1-2, bridg. Parag.). Collas teaches the dissaggregation of rabbit embryos into their blastomere components and incubating the blastomeres, first in colcemid followed by release and synchronization at the G1/S boundary by incubation in aphidicolin (page 494, col. 1, parag. 3, line 7 to col. 2, line 2; and col. 2, parag. 1, lines 1-8). Collas refers to this procedure as "arrest" of embryos in G1 (page 494, col. 2, parag. 2, lines 6-10). Yang teaches the production of rabbit young by nuclear transfer (page 642, Table 4). Collas offers motivation in stating that an enhanced rate of development was seen in nuclear transfer embryos to blastocysts with donor nuclei in the G1 phase, 71% (abstract).

Claims 197 and 228-230 are rejected under 35 U.S.C. 103(a) as being unpatentable over Collas et al (1992) Biol. Reprod. 46, 492-500 in view of Alessi et al (1998) Exp. Cell Res. 245, 8-18 in view of U.S. Patent 5,945,577 issued August 31, 1999 (Stice).

Collas teaches the production of rabbit NT embryos by transferring a donor blastomere cell that had been synchronized at the G1/S boundary into an enucleated oocyte

(page 494, col. 1-2, bridg. Parag.). Collas teaches the dissaggregation of rabbit embryos into their blastomere components and incubating the blastomeres, first in colcemid followed by release and synchronization at the G1/S boundary by incubation in aphidicolin (page 494, col. 1, parag. 3, line 7 to col. 2, line 2; and col. 2, parag. 1, lines 1-8). Collas refers to this procedure as "arrest" of embryos in G1 (page 494, col. 2, parag. 2, lines 6-10). Yang teaches the production of rabbit young by nuclear transfer (page 642, Table 4). Collas offers motivation in stating that an enhanced rate of development was seen in nuclear transfer embryos to blastocysts with donor nuclei in the G1 phase, 71% (abstract). Alessi teaches that olomucine and roscovitine are CDK2 Kinase inhibitors and arrest human fibroblasts in G1 (page 14, col. 2, parag. 1, lines 1-5). Stice specifically describes the culture of fetal fibroblast cells, which are then used as nuclear donors (col. 15, lines 51 to col. 16, line 11 and col. 16, lines 57-60). Stice offers motivation in teaching the cloning of a bovine from fibroblasts (see claims). Thus it would have been obvious to the ordinary artisan to modify the method of Collas where donor blastomeres were arrested in G1, by using as nuclear donors fibroblasts, which had been shown by Stice to served successfully as nuclear donors to produce cloned bovines, using a CDK2 kinase inhibitor such as olomucine or roscovitine given the teachings of Alessi.

Claims 210 215 216 and 217 appear to be free of the prior art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deborah Crouch, Ph.D. whose telephone number is 703-308-1126. The examiner can normally be reached on M-Th, 8:30 AM to 7:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah J. Reynolds can be reached on 703-305-4051. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Deborah Crouch

Deborah Crouch, Ph.D.
Primary Examiner
Art Unit 1632

dc
November 4, 2002